PROGRESS

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MEDICINE.

UNDER THE CHARGE OF
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The Basophilic Granulations of the Red Blood-corpuscles.—O. MORITZ (*Deutsch med. Wochenschrift*, 1901, xxvii., p. 68).

While most authors have been under the impression that the basophilic granulations sometimes observed in the red blood-corpuscles are evidence of degeneration which may have some importance from a diagnostic standpoint, others have believed that they are unimportant artefacts or postmortem phenomena. Grawitz has produced them in mice by heating; Strauss, in frogs and in the rabbit by pyrodin, and Hamel by the feeding of lead to white mice. Moritz, in a series of investigations, succeeded in producing the basophilic granulations in all of five rabbits fed upon pills of acetate of lead, and in one in which the acetate was given subcutaneously. They were found in greater number in two rabbits to whom pyrodin was given subcutaneously. He is further able to support Hamel's observations, that six workers in a lead-color factory, only one of whom had any suspicious signs of lead intoxication, while another had shown symptoms some time before, all showed typical basophilic granulations of the erythrocytes. He has found these granulations also in five other cases: twice in leucæmia, in malaria, sepsis, and carcinoma cachexia.

Excretion of the Bence-Jones Body in the Urine (Albumosuria) in Association with Myelomata of the Ribs.—KALISCHER (*Deutsch med. Wochenschrift*, 1901, xxvii., p. 54).

The patient was a woman, aged sixty-seven years, whose family history was negative; one daughter had died of pernicious anæmia. In July, 1899, the patient began to complain of neuralgic pains in the lower part of the thorax, and of difficulty in breathing. These pains, in the beginning spasmodic, later became permanent and lasted up to the death of the patient.

There were also eructations and nausea, in association with a sensation of præcordial anxiety, coming on without any relation to the taking of food. After December, 1899, the patient was unable to leave her bed on account of the pains which were brought on by walking, sneezing, coughing, or bending, and on account of general weakness. The physicians in charge made a diagnosis of hysteria and neurasthenia. The examinations of the urine were negative, showing only once, toward the end of this period, a trace of albumin. In July, 1900, the patient was first seen by Kalischer. She could not move forward on account of severe pains in the chest, which increased with every step and were continuous, with occasional sharp exacerbations. No abnormalities were to be discovered in the internal organs or central nervous system; the eye-grounds were normal. Sensibility of the skin was normal, except for a hyperalgesia on touching the lower anterior part of the chest. There was especial tenderness over the points of junction of the cartilages and the bones of the fifth, sixth, seventh, and eighth ribs on the left side. There were also some points on the sternum, clavicle, and scapula which were painful on pressure. At that time the only complaints were of a continuous bitter taste in the mouth, loss of appetite, general weakness, and sensation of anxiety. The urine showed an average daily amount of from 1800 to 2000 c.c.; reaction neutral or slightly alkaline; specific gravity 1015; trace of albumin; no casts. On further examination it was found that, on heating the urine to a certain degree, there was a profuse precipitate and clouding, which cleared up on further heating, disappearing entirely on boiling, but coming down again on cooling. There was a profuse precipitate with nitric acid appearing in the cold, dissolving by heat, and appearing again when the urine cooled. The cloudiness appeared at 55° to 60°, the clearing at about 85°. Later a striking softness and bowing, with angular depressions and prominences of the ribs, from the third to the eleventh, became evident; this was especially marked at the junction of the ribs and cartilages. Swollen tender points were noted on the sternum, clavicles, and scapula. Every movement of the arms, mere turning, a deep breath, or too active speaking caused severe attacks of pain. Rapid emaciation, increased anxiety, and fainting attacks followed. Examination of the blood showed a slight increase in the number of leucocytes; nothing remarkable in the red blood-corpuscles. The urine diminished from 600 to 800 c.c. a day. At times albumin was found, but the Bence-Jones body was continuously present up to the time of death, which occurred in the middle of November, about a year and a half after the onset of the disease, resulting from increasing weakness and paralysis of the heart. Only a partial autopsy was allowed. Despite careful handling of the body, palpation showed fractures, depressions, and angular protrusions of the ribs, as well as slight swellings and irregularities of the surface of the ribs, sternum, clavicle, and scapulæ. The ribs felt soft and were abnormally movable. The anterior part of the ribs from the second to the eighth on the left side were removed. They could be readily cut with ordinary scissors, while from the surface a brownish-red pap-like substance similar to splenic pulp welled up. The spongy and compact bone substance of the ribs had almost entirely disappeared, leaving only an external shell as thin as paper. All the ribs were easily broken, and showed various fractures, and, on the left, diffuse clubshaped swellings, or, again, more localized, yellowish elevations from the size of a lentil to the size of a pea, and extensive roughnesses and unevennesses especially on the posterior and lower surfaces. Angular protrusions were also to be felt over the posterior parts of the ribs. Nothing abnormal was noted in the pleuræ, pericardium, heart, or lungs. With the ribs there was also removed a piece of bone from the under part of the right humerus. Here the marrow had its normal color, except for small reddish-brown spots, and neither the compact substance nor the spongiosa had disappeared. There was no widening of the medullary canal. Smear preparations from the marrow and the diffusely diseased ribs showed that, in the ribs, there was a well-marked increase of the colorless round cells without "tumor elements" or foreign structures. The condition might then be assumed to be a hyperplasia of the marrow of lymphoid character (myeloma). The marrow of the humerus was normal microscopically as well as macroscopically. The author points out the similarity of the case to the few others which have been reported in literature.

The Etiology of Yellow Fever.—The preliminary report of Reed and his associates on the etiology of yellow fever has already been reviewed in the February number of this JOURNAL. REED, CARROLL, and AGRAMONTE (*Journal of the American Medical Association*, February 16, 1901, p. 431) recently read a report of their subsequent investigations at the Pan-American Medical Congress, held in Havana, Cuba, February 4 to 7, 1901. Their recent investigations have been directed toward ascertaining the mode of transmission of the disease from individual to individual rather than toward studying the specfic agent of the disease. In their previous report they concluded that the mosquito (culex fasciatus, Fabr.) was responsible for the transmission of the disease. This later work was undertaken largely with the object of confirming these conclusions if possible.

In order to eliminate all possibilities of the disease being contracted from any other source they established a camp, which they called Camp Lazear, in honor of their late colleague, in an open field one mile from the town of Quemados, Cuba. The camp was established on November 20, 1900, after which time it was strictly quarantined, the only persons allowed to leave or enter the camp being three immune members of the detachment and the members of the board. The personnel of the camp consisted of two physicians, one of whom was immune; one immune hospital steward; nine privates of the hospital corps, one of whom was immune, and one immune ambulance driver. A few Spanish immigrants were admitted to the camp from time to time during the investigation. Before the experiments were begun all non-immune individuals were kept in the camp longer than the full period of incubation of yellow fever.

Six non-immune persons were allowed to be bitten by mosquitoes (culex fasciatus) which had previously bitten yellow fever patients. Of these six individuals five contracted yellow fever within the period of incubation of the disease. The negative result was in a case which had been inoculated with a mosquito on the fifteenth day after the insect had bitten a case of yellow fever on the third day. They have an explanation for this negative result, however. They subsequently found that in the case of an insect kept at room temperature during the cool weather of November, fifteen or eighteen days is, in all probability, too short a time to render it capable of producing the disease. Their observations indicated that it takes a certain number of days after the parasite has been taken into the mosquito's stomach before it reaches the salivary glands of the insect and before it can thence be reconveyed into man. This period averages twelve days in summer and eighteen or more days during the cool winter months.

Having, in their minds, conclusively shown that yellow fever can be transmitted by the mosquito they endeavored to ascertain whether it can be conveyed in any other way. Accordingly four individuals were inoculated with blood taken from the general circulation of patients in the acute stage of yellow fever. Three of the four cases developed yellow fever.

They then proceeded to ascertain whether yellow fever can be conveyed by fomites. For this purpose a small frame house consisting of one room 14 x 20 feet was constructed. It was made in such a way as to exclude direct sunlight and mosquitoes. For twenty nights a non-immune physician, Dr. R. P. Cooke, and two non-immune privates of the hospital corps slept in this building. Each night they unpacked and in the morning repacked three large boxes filled with sheets, pillow-slips, blankets, etc., contaminated by contact with cases of yellow fever and their discharges. These articles were hung about the room during the night, and also placed on the bed occupied by Dr. Cooke. At the end of twenty days these three individuals were placed in quarantine for five days and then given their liberty. None of them had developed yellow fever. Subsequently four other individuals for periods of twenty days either slept in the sheets or night clothing which had been contaminated by the discharges of yellow fever patients without contracting the disease.

They then proceeded to demonstrate how house infection with yellow fever occurs. A house similar to the previous one was constructed, only full provision for light and ventilation was made. It was divided into two compartments separated by a wire screen. All articles admitted to this building were first carefully disinfected. In one of the compartments fifteen mosquitoes previously infected by biting yellow fever patients were set free. Two individuals were admitted to the compartment with the mosquitoes and were bitten. One of the two developed yellow fever.

The authors state that at Camp Lazear of seven non-immunes whom they attempted to infect by means of the bites of contaminated mosquitoes they have succeeded in conveying the disease in six, or 85.7 per cent. Out of a total of eighteen non-immunes whom they have inoculated with contaminated mosquitoes, since they began their investigations, eight, or 44.4 per cent., have contracted yellow fever.

The conclusions from their investigations are as follows:

1. The mosquito—c. fasciatus—serves as the intermediate host for the parasites of yellow fever.

2. Yellow fever is transmitted to the non-immune individual by means of the bite of the mosquito that has previously fed on the blood of those sick with this disease.

3. An interval of about twelve days or more after contamination appears to be necessary before the mosquito is capable of conveying the infection.

4. The bite of the mosquito at an earlier period after contamination does not appear to confer any immunity against a subsequent attack.

5. Yellow fever can also be experimentally produced by the subcutaneous injection of blood taken from the general circulation during the first and second days of this disease.

6. An attack of yellow fever, produced by the bite of the mosquito, confers immunity against the subsequent infection of the blood of an individual suffering from the non-experimental form of this disease.

7. The period of incubation in thirteen cases of experimental yellow fever has varied from forty-one hours to five days and seventeen hours.

8. Yellow fever is not conveyed by fomites, and hence disinfection of articles of clothing, bedding, or merchandise, supposedly contaminated by contact with those sick with this disease is unnecessary.

9. A house may be said to be infected with yellow fever only when there are present within its walls contaminated mosquitoes capable of conveying the parasite of the disease.

The Pathology of Herpes Zoster and Its Bearing on Sensory Localization.—HEAD and CAMPBELL (*Brain*, Part III., Autumn, 1900) have recently published a most exhaustive and painstaking study on the above subject. In their introduction to the subject they state that they have determined the pathological lesion which underlies this disease, and have attempted thereby to determine the cutaneous distribution of certain fibres that enter each posterior root ganglion. Bärensprunz, in 1861, was the first to state that herpes zoster was of nervous origin. He was fortunate to secure an autopsy on a case, the study of which led to the universally accepted view that the herpes was associated with a lesion of the posterior root ganglion. The writers point out that although Bärensprunz rightly placed the lesion in the posterior root ganglion, he thought that this structure stood in no connection with the fibres of the posterior root or peripheral nerve, but had special nerve fibres of its own. Up to the time at which Head and Campbell commenced to investigate the pathology of herpes zoster there had been only two well reported autopsies on cases of zoster ophthalmicus and five satisfactory reports on zoster of the trunk. To this number they themselves add twenty-one cases at all stages after the eruption. The authors divide their report into three parts. In Part I. they take up the pathology of herpes zoster.

The changes in the ganglion of the posterior roots vary according as to whether they are acute or chronic. The acute changes consist of (1) extremely acute inflammation with the exudation of small round deeply-staining cells; (2) extravasation of blood; (3) destruction of ganglion cells and fibres; (4) inflammation of the sheath of the ganglion. If severe such a condition eventually leaves a scar in that part of the ganglion affected and leads to thickening of the sheath over the affected area. On the other hand, if the eruption has not been severe all traces of the inflammation present in the acute stage may pass away, leaving the ganglion apparently normal.

The changes in the posterior nerve roots are somewhat similar. They consist of an acute degeneration followed by a greater or less amount of secondary sclerosis according to the severity of the acute destruction. The anterior root was always normal.

In the peripheral nerves they state that degeneration seems to appear, to disappear, and to be replaced by sclerotic changes at the same periods after the initial lesion in the ganglion, as was the case with the posterior roots.

The changes in the spinal cord are practically the same as those which follow division of a posterior root or excision of a posterior root ganglion experimentally. There is an acute degeneration of the root fibres in the posterior columns of the cord from the point of entrance of the fibres from the involved root.

Zoster of the branches of the trigeminal is associated with a similar lesion in the Gasserian ganglion to that found in the posterior root ganglion in cases of zoster of the trunk and limbs. This lesion causes secondary degeneration in the sensory root of the Gasserian ganglion, both in its extramedullary and intramedullary course.

The authors state that a herpes zoster, in all respects resembling that arising spontaneously, may be produced by implication of a posterior root ganglion in inflammatory processes secondary to malignant disease, tubercle or injury. They also refer to the occasional appearance of herpes in cases of organic diseases of the nervous system. A short chapter is devoted to a consideration of the changes in the skin and lymphatic glands. They point out the curious fact that although the serum of the vesicles is sterile yet there is enlargement of the associated lymphatic glands.

An interesting chapter is devoted to a discussion of herpes zoster as an acute infectious disease of the nervous system. It has its prodromal period in which fever and pain may be the only symptoms. With the appearance of the rash the disease declares itself. They compare the disease to acute lobar pneumonia. The rash in herpes appears generally on the third or fourth day, just as the physical signs of pneumonia become well marked usually on the third or fourth day. Other evidences in favor of the infectious character of the disease are the infrequency of second attacks, and the occurrence of definite epidemics. They have met with only four instances of second attacks in over four hundred cases, and they have repeatedly noted the tendency of the disease to prevail at certain periods.

They draw an analogy between anterior poliomyelitis and herpes zoster. Just as in the former the unknown poison picks out the motor cells in the anterior horns, so in herpes zoster the unknown poison selects the posterior root ganglia. From a table compiled from 392 cases they show that the ganglia most commonly affected are those which receive afferent impulses from the viscera through the white ramus of the sympathetic. The posterior root ganglia contain two types of cells, large, coarsely-granular nerve cells and smaller more pear-shaped cells, which stain more uniformly with methylene-blue. They find that in herpes zoster the ganglia which are most frequently involved are those which contain a preponderance of the small cells, which give rise to the shorter fibres of the posterior columns of the cord. These small cells, among other functions, are believed to subserve pain, as Münzer has shown that the long tracts of the posterior columns do not conduct pain impressions to the cerebrum. Hence the intense pain which accompanies an attack of herpes zoster. They do not believe that the eruption of herpes zoster is produced by disturbance of special trophic nerves, but by intense irritation of cells in the ganglion which normally subserve the function of pain, and more particularly that form of pain produced by afferent visceral impulses.

In Part II. the writers discuss the bearing of the distribution of the eruption in herpes zoster on sensory localization. Before they began this research Head had collected a large number of cases of herpes zoster, and had constructed a diagram to show the relation that the areas occupied by the eruption bore to one another. A series of segments was thus mapped out upon the surface of the body, and to each segment was given a hypothetical number which was supposed to represent its numerical localization in the central nervous system. This numerical localization met with universal disbelief alike from anatomists and clinicians, and Head felt that if a post-mortem could be obtained on a case of herpes zoster in which the distribution of the eruption had been carefully drawn or photographed the question might be settled one way or another. Head and Campbell eventually were able to secure autopsies on twenty-one cases of herpes thus previously studied. This material has enabled them to deal with the question of numerical localization in a complete manner. In their diagram and in the text the name used to designate the skin areas refer to a definite posterior root ganglion. Thus " the fourth dorsal " area means that that area corresponds with disturbance of the fourth dorsal ganglion. The clinical study of these cases, with the confirmation obtained from the post-mortem, showed that their original diagram of the areas was in its main essentials correct. They show that these areas may vary markedly in different individuals, owing to variations in the surface from stretching of the skin, as in the mammary region, without any necessary alterations in nerve supply.

In conclusion, they believe that when a certain ganglion is affected the eruption most frequently lies over a definite tract of skin, which may be called the normal area from which fibres enter that ganglion. This tract of skin may, however, in some cases be situated further headwards, and occupy about one-half or less of the area usually supplied by the segment in front (pre-fixed). It may be situated further toward the " tail end " of the body (post-fixed) to the same extent. But its displacement never exceeds half an area in either direction, and in no case did they find that an eruption, which lay over what they supposed to be the complete normal area of a certain segment, was produced by a lesion of either the ganglion above or the ganglion below. They found, further, that the areas marked out by the eruption of herpes zoster overlap one another to a very variable extent. On the trunk this overlap was slight when individual differences and variation in nerve supply were taken into account. In the neck the overlap consisted more of a sharing of a certain territory than of true overlap, but on the limbs the overlapping was distinct. In no case did the overlap equal in extent more than one-half of the area above and below, while in many cases it was considerably less.

Part III. contains the clinical and post-mortem reports of their twenty-one cases of herpes zoster in which they secured autopsies, and from which they drew their conclusions already given. The report is accompanied by numerous figures and seventeen plates.